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European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
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— of inventorship (Rule 4.17(iv)) for US only

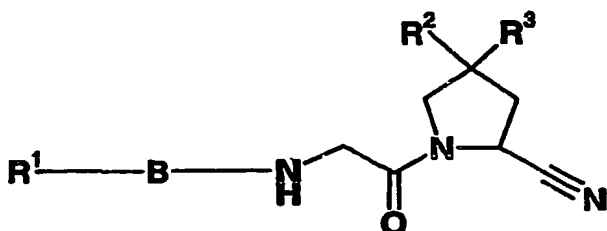
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(54) Title: N-AMINOACETYL-PYRROLIDINE-2-CARBONITRILES AND THEIR USE AS DDP-IV INHIBITORS



(I)

(57) Abstract: The present invention relates to new, potent DPP-IV enzyme inhibitors of the general formula (I), which contain fluorine atoms.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/HU 03/00017

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D451/04 C07D451/14 C07D401/14 C07D417/14 C07D413/14
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 C07D211/58 A61K31/46 A61K31/395 A61K31/497 A61K31/4545

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01 96295 A (NOVARTIS AG ET AL) 20 December 2001 (2001-12-20) the whole document	1-29
X	page 34, example 2kk	23
Y	WO 98 19998 A (NOVARTIS AG) 14 May 1998 (1998-05-14) the whole document	1-29
X	page 12, example 17, page 14, example 66	23
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

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- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
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- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

15 July 2003

Date of mailing of the international search report

24 07 2003

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/HU 03/00017

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/505 A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	AUGUSTYNS KJL ET AL: "Pyrrolidides: synthesis and structure-activity relationship as inhibitors of dipeptidyl peptidase IV" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, vol. 32, no. 4, 1997, pages 301-309, XP004086653 the whole document, particularly compounds 17b and 18b, and page 303, right-hand column, 2nd paragraph	1-29
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P, X	page 22, formula 9	26, 27
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

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- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
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Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/HU 03/00017

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 03 002553 A (SMITHKLINE BEECHAM CORPORATION) 9 January 2003 (2003-01-09) the whole document ---	1-29
X	US 4 001 422 A (DANILEWICZ JC ET AL) 4 January 1977 (1977-01-04) examples 2 and 4 ---	25
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; XP002242778 Beilstein Registry Number 6688440 & J. MED. CHEM., vol. 36, no. 23, 1993, pages 3707-3720, ---	25
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/HU 03/00017

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/HU 03/00017

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 156 433 A (JANSSEN PHARMACEUTICAL N.V.) 2 October 1985 (1985-10-02) example 40 ---	23
X	WO 99 65895 A (SANOFI-SYNTHELABO) 23 December 1999 (1999-12-23) examples 7 and 8 ---	23, 25
P, Y	WO 02 30890 A (TANABE SEIYAKU CO., LTD.) 18 April 2002 (2002-04-18) the whole document P, X page 90, compounds 7-1, 7-3 and 7-7	1-23, 25, 29
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P, X	WO 03 000250 A (FERRING BV) 3 January 2003 (2003-01-03) example 1D ---	26
P, X	WO 03 002531 A (SMITHKLINE BEECHAM CORPORATION) 9 January 2003 (2003-01-09) Intermediate examples 1E and 2C -----	26

INTERNATIONAL SEARCH REPORT

International application No.
PCT/HU 03/00017

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 23, 25 (both partly)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 23, 25 (both partly)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty of claims 23 and 25. So many documents were retrieved that it is impossible to determine which parts of these claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT).

For these reasons it appears impossible to execute a meaningful search and/or to issue a complete search report over the whole breadth of said claims.

The search and the report for said claims can only be considered as complete for compounds wherein R1 has the meanings recited in claims 8-12.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-23, 25, 29

N-substituted 1-aminoacetyl-2-cyano-pyrrolidines, their use and preparation, and amines

2. Claims: 24, 26-28

Pyrrolidines

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/HU 03/00017

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/HU 03/00017

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